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EXAMINER
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DATE MAILED: 07/07/92

This is a communication from the examiner in charge of your application
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 4/29/92 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

**Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:**

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

**Part II SUMMARY OF ACTION**

1. ☒ Claims 1-44 are pending in the application.
   Of the above, claims 1-9, 13, 29, 40 & 41 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 10, 11, 12, 14-28, 30-39 & 42-44 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

15. Applicant's election with traverse of Group II in Paper No. 7 is acknowledged. The traversal is on the ground(s) that the claims of group I are drawn to isolated DNA encoding Cry j I protein or fragments thereof. The DNA sequence of claims 1-9, 13 and 29 when expressed is the same allergenic protein or peptide of Japanese Cedar pollen of claims 10-12, 14-28, 30-39 and 42-44. thus, there appears to be a relationship between Groups I and II which precludes them from being termed "independent". This is not found persuasive because as stated in the first office action the inventions of Group I and Group II are related as process of making and product made. Therefore the inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (M.P.E.P. 806.05(f)). In the instant case number (2) applies. It was shown that the product can be made by direct purification from the source, or by chemical synthesis. It was further stated that the two groups are distinct with respect to their structure, physical properties, and function and are therefore novel and unobvious in view of each other and are patentably distinct. Further Group III was not addressed and is therefore considered as an election with out traverse with respect to Group III.

The requirement is still deemed proper and is therefore made FINAL.

## REJECTIONS WHICH STILL REMAIN

16. 35 U.S.C. 101 reads as follows:
"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

17. Claims 10-12, 14-28, 30-39 and 42-44 are rejected under 35 U.S.C. 101 because (b) the claimed invention lacks patentable utility. b) The invention is claimed to have therapeutic applications. However, U.S. Patent No. 4939239, column 1, lines 37-51, point out that the use of intact cedar pollen allergen has been attempted to effect hyposensitization of cedar pollinosis affected individuals, but has sever drawbacks. Particularly the potential of eliciting anaphylaxis, and the care needed in . . . "handling it because it is readily adsorbed on vessels such as glassware and metalware, ... which renders the administration of the prescribed amount of cedar pollen allergen very difficult". These references make the patentable utility of the present invention questionable. The present invention may do more harm than good. Further, applicants have provided no in-vivo or in-vitro data. Pharmaceutical therapy is unpredictable in the absence of in-vivo clinical data for the following reasons:

1) The protein/fragment may be inactivated before producing an effect, e.g. such as proteolytic degradation, immunological inactivation or due to an inherently short half life of the protein/fragment,

2) A large enough effective local concentration may not be capable of being established,

3) Other functional properties, known or unknown, may make the protein/fragment unsuitable for in-vivo use, the protein/fragment may produce adverse side effects prohibitive to the use of such treatment, as discussed above. See MPEP 608.01(p).

Applicant is encourage to file a rule 132 declaration to provide objective statistically significant evidence commensurate with the scope of the claims showing the operability of the therapeutic composition claimed, see 37 C.F.R. 1.132 and MPEP 716.

18. The disclosure is objected to because of the following informalities:

a) The specification should be amended to recite 07/729134, page 1 line 9, as the correct serial number of the parent application.

b) The sequences in the specification should have an orientation markers, for example, 5' and 3' for nucleotide sequences or NH2 and COOH for amino acid sequences, to allow immediate recognition of the correct orientation of the sequence.

Appropriate correction is required.

19. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

20. The specification is objected to under 35 U.S.C. 112, first paragraph, as failing to provide an adequate written description of the invention and failing to adequately teach how to make and use the invention. The specification failed to enable the therapeutic application of the invention for the same reasons as that given in above paragraph #17.

21. Claims 10-12, 14-28, 30-39 and 42-44 rejected under 35 U.S.C. 112, first paragraph, for the reasons set forth in the

objection to the specification.

22. Claims 10-12, 14-18, 25-25, 30, 32, 33, 36-39 and 42-44 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

b) Claims 10, 12, 14-18, 32, 33, 36-39, 42-44 are indefinite in the recitation of the phrase "at least one". The phrase represents a very large number of fragments. The claims are required to be amended to recite distinctly which fragments are being claimed. The amendment must point to support in the specification so as not to add new matter.

d) Claims 30 and 32 are indefinite in the recitation of the term "reduces". It is unclear to what degree the protein will reduce. Amendment of the claims is required to distinctly point out what level of reduction is being claimed. The amendment must point to support in the specification so as not to add new matter.

e) Claims 38 and 39 are indefinite in the recitation of the phrase "a therapeutically effective amount". It is not clear what amount represents a therapeutically effective amount. Amendment of the claims is required to distinctly point out what amount is being claimed. The amendment must point to support in the specification so as not to add new matter.

f) Claim 42 is indefinite in the recitation of the phrase "down regulation". It is unclear what level of down regulation is being claimed. Amendment of the claims is required to distinctly point out what amount of down regulation is being claimed. The amendment must point to support in the specification so as not to add new matter.

g) Claim 44 is indefinite in the recitation of the phrase "sufficient quantity". It is unclear what a sufficient quantity represents. Amendment of the claims is required to distinctly point out what quantity is being claimed. The amendment must point to support in the specification so as not to add new matter.

23. Claims 10-12, 14-20, 23, 26-28, 30-39 and 42-44 rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 4939239, ('239). '239 anticipates the invention by disclosing a method of purifying the same cedar pollen allergen, column 4, lines 15-58, as the present invention. The invention defined in a product-by-process claim is a product, not a process. In re Bridgeford, 357 F2d 679, 149 U.S.P.Q. 55 (CCPA 1966). It is the patentability of the product claimed and NOT of the recited process steps which must be established. In re Brown, 459 F2d 531, 173 U.S.P.Q. 685 (CCPA 1972); In re Wertheim, 541 F2d, 191 U.S.P.Q. (CCPA 1976). A comparison of the recited process with

the prior art processes does NOT serve to resolve the issue concerning the patentability of the product. In re Fessman, 489 F2d 742, 180 U.S.P.Q. 324 (CCPA 1974). Whether a product is patentable depends on whether it is known in the art or it is obvious, and is not governed by whether the process by which it is made is patentable. In re Klug, 333 F2d 905, 142 U.S.P.Q. 161 (CCPA 1964). In an ex parte case, product-by-process claims are NOT construed as being limited to the product formed by the specific process recited. In re Hirao et al., 535 F2d 67, 190 U.S.P.Q. 15, see footnote 3 (CCPA 1976). Therefore, the method of purification is moot. Further, '239 discloses that the protein is antigenic, column 4, line 40, it binds IgE. '239, claim 2, discloses a sequence, from this methods are known in the art to synthesize this fragment. The protein has minimal IgE stimulating activity, column 12, lines 13-22, and is capable of modifying the sensitivity to cedar pollen see column 8, line 62- to- column 9, line 3, and therefore reduces the allergic response, see abstract. '239 discloses a modified protein, see abstract. Therefore, '239 encompasses the entire claimed invention.

24. Claims 21, 22 and 24 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103 as obvious over '239. As discussed in above paragraph #29, '239 discloses a purified cedar pollen antigen, teaches a amino terminal sequence, and discloses methods of using the purified antigen. Since the cedar pollen protein is an allergen, stimulation of T-cells represents an inherent property of the protein. Further, since '239 discloses the entire protein basic enzymatic degradation, which is well known in the art, would be capable of producing antigenic fragments which do not bind IgE.

## RESPONSE TO APPLICANTS ARGUMENTS:

25. The rejection of claims 10-12, 14-28, 30-39 and 42-44 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter has been withdrawn in response to applicants remarks.

26. The rejection of claims 30-33, 36-39 and 42-44 under 35 U.S.C. 101 because the claimed invention lacks patentable utility, still stands. Applicants strongly disagree with the observation in view of Matsuhashi, et al., that the present invention does more harm than good. Stating "that despite some of the drawbacks of standard immunotherapy, this method of treating allergy is still considered useful and has been used successfully to treat many allergy patients. The present invention further decreases the possibility of anaphylaxis during immunotherapy and therefore improves the chances that the associated drawbacks of using cedar pollen extract will not occur".

Applicants continue "Furthermore, the attendant problems described by Matsuhashi, et al., regarding working with whole purified native pollen is not an issue as one skill in the art is capable of determining which stabilizer, buffers or other pharmaceutical agents would be capable of preventing this problem". Applicants argue that the therapeutic uses of the present invention are not unpredictable. Pointing to the specification at pages 10 and 11, applicants state "Cry j I protein allergen or fragments thereof of the present invention can be administered for therapeutic purposes such as in standard immunotherapy. As discussed above, although there are certain drawbacks, native protein allergens have been used successfully to treat allergy patients. Additionally, with respect to the peptides of the invention, other investigators have suggested the use of peptic fragments of a protein for immunotherapy". Applicants have however not addressed the specific components of the rejection. Specifically, there is no in-vivo or in-vitro data. As stated in the first office action pharmaceutical therapy is unpredictable in the absence of in-vivo clinical data for the following reasons:

1) The protein/fragment may be inactivated before producing an effect, e.g. such as proteolytic degradation, immunological inactivation or due to an inherently short half life of the protein/fragment,

2) A large enough effective local concentration may not be capable of being established,

3) Other functional properties, known or unknown, may make the protein/fragment unsuitable for in-vivo use, the protein/fragment may produce adverse side effects prohibitive to the use of such treatment, as discussed above. See MPEP 608.01(p).

This information is critical especially when the therapeutic value of the invention is in question, as is the case in the instant application with respect to Matsuhashi, et al. Merely stating that the invention has therapeutic value is not convincing evidence that the unpredictable problems discussed in the above numbers 1-3 have been overcome. Applicants have not provided any statistically significant data, supporting the utility of the claimed invention.

27. The objection to the disclosure because of informalities, still stands. Applicant states on page 5, lines 1-2 of the remarks that the informalities have been corrected. There is no amendment in the response correcting these informalities. Therefore applicant is held non-responsive with regard to these objections.

28. The objection to the specification under 35 U.S.C. 112,

first paragraph, as failing to provide an adequate written description of the invention and failing to adequately teach how to make and use the invention, still stands. Applicants state "In view of the above discussion, (response to 101 rejection), applicants respectfully submit that the specification is enabling for therapeutic use of the present invention". Applicants have not disclosed to one of ordinary skill in the art how to use the protein as a pharmaceutical or therapeutic agent. There is an insufficient written description of the invention with respect to the in vivo operability of the protein to enable one of ordinary skill in the art to use applicant's invention, for the reasons discussed in detail in the previous rejection made under 35 U.S.C. 101. Furthermore, applicant has provided no teaching or guidance indicating what dosages are required and what way(s) the protein can be administered (see Ex parte Powers, 220 U.S.P.Q. 924 (Bd. Pat. App. & Int. 1982)) or otherwise used in a practical manner. It would, therefore, require undue experimentation of one of ordinary skill in the art to determine how to use the claimed protein for the reasons previously discussed. See Ex parte Forman, 230 U.S.P.Q. 546 (Bd. Pat. App. & Int. 1986).

29. The rejection of claims 30-33, 36-39 and 42-44 under 35 U.S.C. 112, first paragraph, for the reasons set forth in the objection to the specification, still stands.

30. The rejection of claims 10, 11 and 12 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, has been withdrawn in response to applicants remarks. Claims 10, 11, and 12 are indefinite in the recitation of the term "purified" it is unclear to what degree of purity the term refers to. The claims are required to be amended to recite the degree of purity being claimed. The amendment must point to support in the specification so as not to add new matter.

31. The rejection of claims 10, 12, 14-18, 32, 33, 36-39 and 42-44 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, still stands. Applicants state that they "are the first to determine the entire nucleic acid sequence which codes for the Japanese cedar pollen allergen Cry j I, and the first to disclose the amino acid sequence. Once the entire nucleic acid sequence has been determined and the protein sequence deduced therefrom, any number of fragments of that protein can be produced recombinantly or synthetically. To limit applicants to only particular fragments would be unduly restrictive and not reflect applicants' contribution to the art". Applicant is directed to the teachings of Yasueda, et al. Yasueda, et al., teach the isolation and

partial characterization of the major allergen from Japanese cedar pollen. No precise sequence was identified but at least one fragment of the allergen was isolated. Therefore applicants are required to definitively recite which fragments are being claimed. Whether applicants' are the first to sequence the protein is a moot point.

32. The rejection of claims 25-28 and 42 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn, in response to applicants amendments.

33. The rejection of claims 30-32 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, still stands. "Applicants respectfully submit that it is clear to one skilled in the art that reduction of the allergic response of the individual to Japanese Cedar pollen allergen can be determined by standard clinical procedures". This may be true, however there is not statement as to what level of reduction is intended. The problem arises if this protein only reduces the allergic response 5%, but another yet to be identified protein reduces the allergic response 100%. If this current claim were allowable it would render the newly identified protein obvious. Further a person of ordinary skill in the art would be unduly burdened to determine at what level of reduction of the allergic response represents maximal reduction. Therefore the claim is required to definitively state the level of reduction intended.

34. The rejection of claims 38 and 39 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, still stands. Applicants point to page 11, lines 21-26 of the specification and state that "as is well known in the art, therapeutically effective amounts of the compositions of the invention will vary according to a number of factors. It is believed that one skilled in the art would be capable of determining an appropriate therapeutic dosage". As stated above in the objection to specification under 35 U.S.C. 112, first paragraph, it would require undue experimentation of one of ordinary skill in the art to determine how to use the claimed protein for the reasons previously discussed, which refers to dosages. See Ex parte Forman, 230 U.S.P.Q. 546 (Bd. Pat. App. & Int. 1986). Applicant admits that therapeutically effective amounts of compositions of the invention will vary according to a number of factors but they have not even provided a reasonable starting point.

35. The rejection of claim 42 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, still stands. Applicants state that "it would be unduly restrictive to limit the present invention to a particular level of down regulation as one skilled in the at would be capable of determining when statistically significant down regulation of the immune system has occurred when using the present invention". Again the problem arises if this protein down regulates the immune response 5%, but another yet to be identified protein down regulates the immune response by 100%. If this current claim were allowable it would render the newly identified protein obvious. Therefore the claim is required to definitively state the level of down regulation intended. A person of ordinary skill in the art would be unduly burdened to determine if the treatment was effective and at what level of down regulation was maximal. Therefore the claim is required to be amended to definitively state what level of down regulation is intended.

36. The rejection of claim 44 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, still stands. "Applicants submit that it is clear to one skilled in the art that the amount of Japanese cedar pollen allergen necessary to provoke a response indicative of sensitivity in accordance with the method of claim 44 will vary depending on a number of factors including the degree of sensitivity of the individual to Japanese cedar pollen, the age and the sex of the individual". Applicants fail to provide any indication of what a sufficient quantity. A person of ordinary skill in the art would be unduly burdened determining what quantity of allergen is sufficient. Applicant has not even provided a starting point.

37. The provisional rejection of claims 1-44 under 35 U.S.C. 101 as claiming the same invention as that of claims 1-44 of copending application Serial No. 07/729134, has been withdrawn in response to the abandonment of the copending application.

38. The rejection of claims 10-12, 14-20, 23, 26-28, 30-39 and 42-44 rejected under 35 U.S.C. 102(b) as being anticipated by Matsuhashi, et al., United States Patent No. 4939239, still stands. Applicants argue that "It is well known that there are a number of structural differences between the native form of a protein and the recombinantly or synthetically produce non-native form of that same protein". Applicant is speaking generically, possibly making reference to the fact that glycosylated proteins are not glycosylated when expressed in bacterial systems. However, other systems such as those suggested to be used

applicant such as yeast and insect cells will gylcosylate and modify proteins the same as found in nature, see specification page 7, lines 15-16. Further it is unclear from the specification as to whether these structural differences if any occur on the protein in question and if they effect the claimed invention. Applicants also state that "without the disclosure by Matsuhashi, et al., of the entire nucleic acid sequence or deduced amino acid sequence of the Japanese cedar pollen allergen, there is no way of knowing which of the allergens from Japanese cedar pollen Matsuhashi and co-workers have purified". Sakagughi, et al, is referred to here as a background reference. Sakagughi, et al., purified and characterized a second Japanese cedar pollen, referred to as Cry j II. Notice table 1 on page 310. The two protein, Cry j I and Cry j II, sequences are compared. Notice the lack of sequence homology between the two sequences. There is therefore no reason to expect that Matsuhashi, et al., have purified a different allergen from the currently claimed. The sequence disclosed by Matsuhashi, et al., is exactly the same as that disclosed in the instant application. Considering the divergence between Japanese cedar pollen allergens the Matsuhashi, et al., allergen is exactly the same as that currently claimed. Applicants bear the burden of providing evidence to demonstrate that the claimed protein is different from Matsuhashi, et al. Applicants reliance upon the way in which the protein was purified is moot with respect to the statement previously made of record. Specifically, the invention defined in a product-by-process claim is a product, not a process. In re Bridgeford, 357 F2d 679, 149 U.S.P.Q. 55 (CCPA 1966). It is the patentability of the product claimed and NOT of the recited process steps which must be established. In re Brown, 459 F2d 531, 173 U.S.P.Q. 685 (CCPA 1972); In re Wertheim, 541 F2d, 191 U.S.P.Q. (CCPA 1976). A comparison of the recited process with the prior art processes does NOT serve to resolve the issue concerning the patentability of the product. In re Fessman, 489 F2d 742, 180 U.S.P.Q. 324 (CCPA 1974). Whether a product is patentable depends on whether it is known in the art or it is obvious, and is not governed by whether the process by which it is made is patentable. In re Klug, 333 F2d 905, 142 U.S.P.Q. 161 (CCPA 1964). In an ex parte case, product-by-process claims are NOT construed as being limited to the product formed by the specific process recited. In re Hirao et al., 535 F2d 67, 190 U.S.P.Q. 15, see footnote 3 (CCPA 1976). Matsuhashi, et al., therefore anticipates the claimed invention.

39. The rejection of claims 21, 22 and 24 under 35 U.S.C. 103 as obvious over Matsuhashi, et al, still stands. Applicants disagree. Stating "there is not suggestion in Matsuhashi that would lead one to use protein degradation to produce antigenic fragments. Furthermore the structural information of the Cry j I protein is necessary in order to design fragments capable of

modifying the immune response to Japanese cedar pollen", citing page 13, line 29 to page 14, line 29. Applicants further state that it is almost impossible to reproduce the exact sam peptides in every degradation experiment even if the same enzyme degradation scheme is used each time and once the peptides were obtained it would be difficult to purify the mixture of peptides. The structural information of the Cry j I is not necessary to design fragments capable of modifying the immune response to Japanese cedar pollen the fragments can be obtained from basic enzyme hydrolysis. Applicants state enzyme hydrolysis is unpredictable. Proteolytic enzymes are known to a person of ordinary skill in the art to recognize specific consensus sequences. Therefore they are not unpredictable and would result in the generation of the same fragments consistently. If the enzymes result in different fragments there are extensive reports in the scientific literature which are now incorrect. These reports rely on the generation of specific consistent cleavages of proteins by the use of specific proteolytic enzymes, one method in particular which uses this type of fragmentation is the Cleveland method. Further, many protein databases have the capacity to predict where specific proteolytic cleavage sites exist on proteins these databases would not be able to predict this type information unless the enzymes consistently cleaved the protein at a specific consensus cite. Applicants statement that it would be almost impossible to reproduce the exact same peptides in every degradation experiment even if the same enzyme degradation scheme is used is moot. Second the idea that it is very difficult to purify peptides, is moot. Methods exist which allow for the purification of peptides a person of ordinary skill in the art would have been motivated to develop the a method which purifies the peptide of interest. This type of purification is a routine procedure in almost every scientific laboratory, interested in proteins. Further, once a particular protein or peptide was isolated it could have been sequences using standard method and from this information peptides could be synthesized by standard methods. Notice that the restriction requirement relied on the fact that proteins can be chemically synthesized. A person of ordinary skill in the art would have been motivated to obtain fragments which do not bind IgE, so as to a protection from an allergic response. Therefore the claimed invention is completely encompassed by Matsuhashi, et al., and is very clearly prima facie obvious.

40. No claims are allowed.

41. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS

ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

42. Papers related to this application may be submitted to Group 180 by facsimile transmission. Papers should be faxed to Group 180 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4227.

43. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donald E. Adams whose telephone number is (703) 308-1834. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 180 receptionist whose telephone number is (703) 308-0196.

July 1, 1992

Donald E. Adams, Ph.D. DEA

Y. CHRISTINA CHAN
PRIMARY EXAMINER
GROUP 180